

What is claimed is:

1. A method for determining the sequence of a DNA,
wherein (i) about 1000 or fewer copies of the DNA
5 are bound to a solid substrate via 1,3-dipolar
azide-alkyne cycloaddition chemistry and (ii) each
copy of the DNA comprises a self-priming moiety,
comprising performing the following steps for each
nucleic acid residue of the DNA to be sequenced:
10 (a) contacting the bound DNA with DNA polymerase
and four photocleavable fluorescent nucleotide
analogues under conditions permitting the DNA
polymerase to catalyze DNA synthesis, wherein
(i) the nucleotide analogues consist of an
15 analogue of G, an analogue of C, an analogue of
T and an analogue of A, so that a nucleotide
analogue complementary to the residue being
sequenced is bound to the DNA by the DNA
polymerase, and (ii) each of the four analogues
20 has a pre-determined fluorescence wavelength
which is different than the fluorescence
wavelengths of the other three analogues;
(b) removing unbound nucleotide analogues; and
(c) determining the identity of the bound
25 nucleotide analogue,
thereby determining the sequence of the DNA.
2. The method of claim 1, further comprising the step
of photocleaving the fluorescent moiety from the
30 bound nucleotide analogue following step (c).

3. The method of claim 1, wherein the solid substrate is glass or quartz.
4. The method of claim 1, wherein fewer than 100 copies of the DNA are bound to the solid substrate.
5. The method of claim 1, wherein fewer than 20 copies of the DNA are bound to the solid substrate.
- 10 6. The method of claim 1, wherein fewer than five copies of the DNA are bound to the solid substrate.
7. The method of claim 1, wherein one copy of the DNA is bound to the solid substrate.
- 15 8. A method for determining the sequence of an RNA, wherein (i) about 1000 or fewer copies of the RNA are bound to a solid substrate via 1,3-dipolar azide-alkyne cycloaddition chemistry and (ii) each copy of the RNA comprises a self-priming moiety, comprising performing the following steps for each nucleic acid residue of the RNA to be sequenced:
 - 20 (a) contacting the bound RNA with RNA polymerase and four photocleavable fluorescent nucleotide analogues under conditions permitting the RNA polymerase to catalyze RNA synthesis, wherein
25 (i) the nucleotide analogues consist of an analogue of G, an analogue of C, an analogue of U and an analogue of A, so that a nucleotide analogue complementary to the residue being
30 sequenced is bound to the RNA by the RNA polymerase, and (ii) each of the four analogues

- has a pre-determined fluorescence wavelength which is different than the fluorescence wavelengths of the other three analogues;
- (b) removing unbound nucleotide analogues; and
- 5 (c) determining the identity of the bound nucleotide analogue,
- thereby determining the sequence of the RNA.
9. The method of claim 8, further comprising the step
- 10 of photocleaving the fluorescent moiety from the bound nucleotide analogue following step (c).
10. The method of claim 8, wherein the solid substrate
- is glass or quartz.
- 15 11. The method of claim 8, wherein fewer than 100 copies of the RNA are bound to the solid substrate.
12. The method of claim 8, wherein fewer than 20 copies
- 20 of the RNA are bound to the solid substrate.
13. The method of claim 8, wherein fewer than five copies of the RNA are bound to the solid substrate.
- 25 14. The method of claim 8, wherein one copy of the RNA is bound to the solid substrate.
15. A composition of matter comprising a solid substrate having a DNA bound thereto via 1,3-dipolar azide-
- 30 alkyne cycloaddition chemistry, wherein (i) about 1000 or fewer copies of the DNA are bound to the

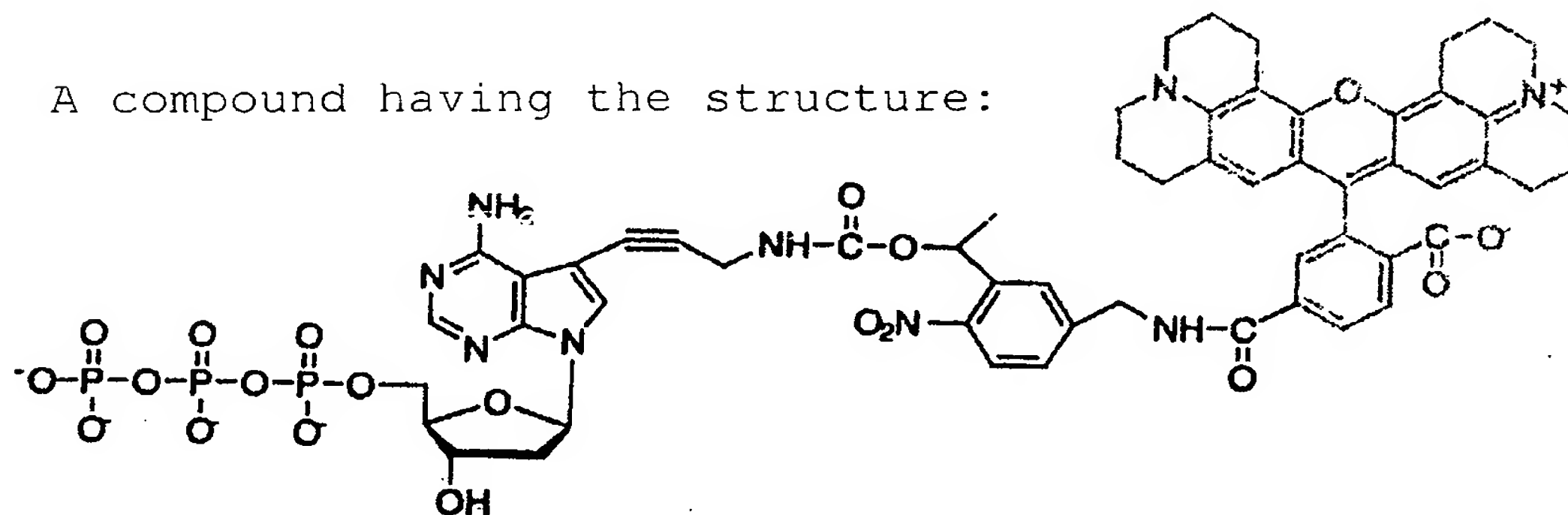
solid substrate, and (ii) each copy of the DNA comprises a self-priming moiety.

16. A composition of matter comprising a solid substrate having a RNA bound thereto via 1,3-dipolar azide-alkyne cycloaddition chemistry, wherein (i) about 1000 or fewer copies of the RNA are bound to the solid substrate, and (ii) each copy of the RNA comprises a self-priming moiety.

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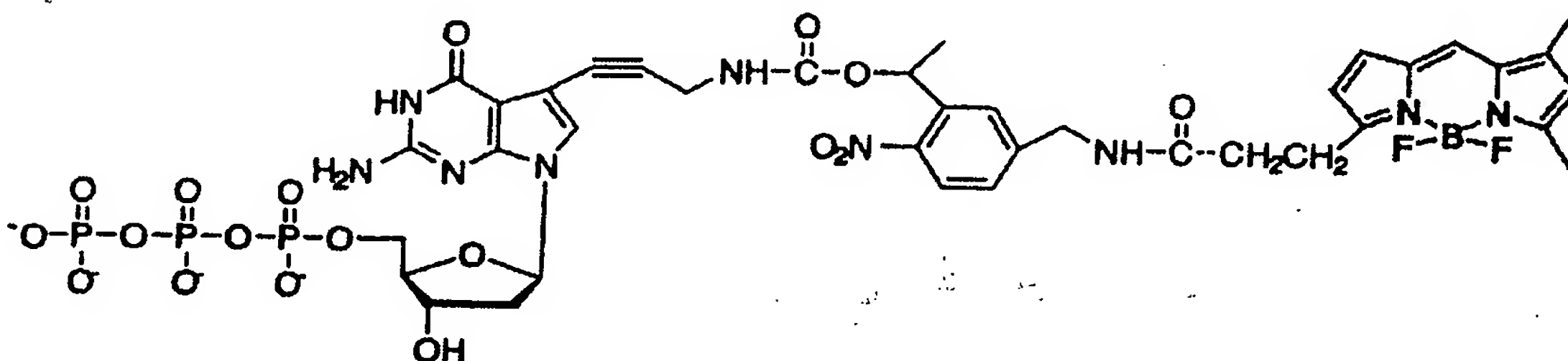
17. A compound having the structure:

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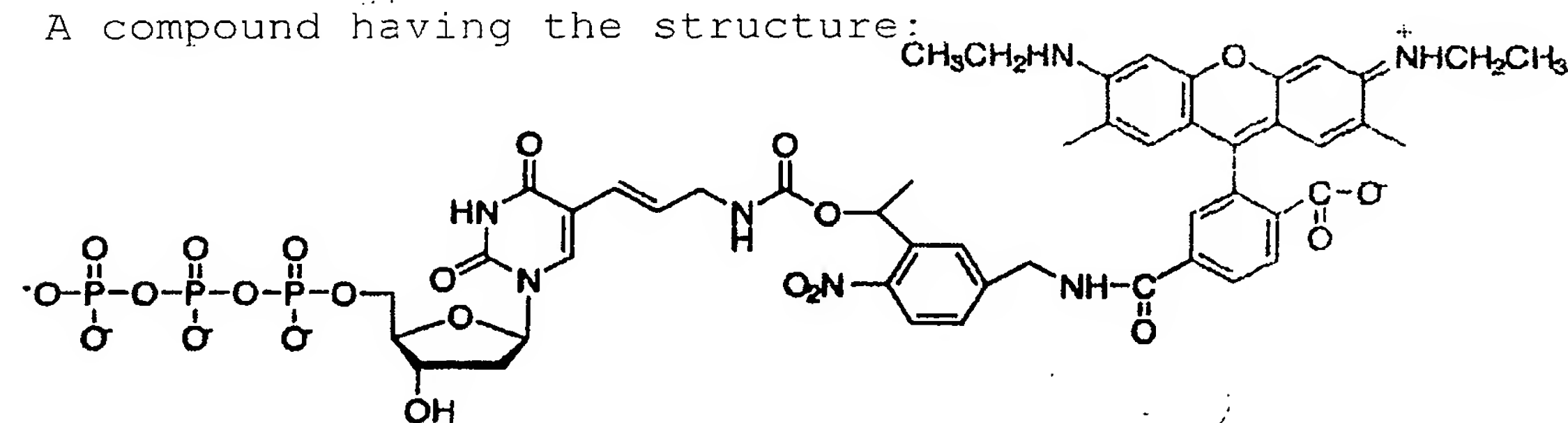
18. A compound having the structure:

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19. A compound having the structure:

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20. A compound having the structure:

